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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/738,478

12/17/2003

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EXAMINER

GAMBEL, PHILLIP

ART UNIT

PAPER NUMBER

1644

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

12/18/2006

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/738,478	Applicant(s) CUMMINGS ET AL.	
	Examiner Phillip Gambel	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2 and 3 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2 and 3 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's amendment, filed 10/10/06, has been entered.

Claim 1 has been canceled.

Claim 3 has been added.

Claims 2-3 are pending.

2. Applicant's election of Group II without traverse in the Response To Notice To Restriction Requirement And Amendment, filed 10/10/06 is acknowledged.

However, given the cancellation of claim 1, the Restriction Requirement has been rendered moot.

Applicant's election of the specific disorder, wherein the specific disorder involves defective binding of the leukocytes to activated platelets or endothelial cells, is acknowledged.

While the examiner was seeking an election of a particular disease/disorder (e.g., rheumatoid arthritis described in Clinical Applications on pages 44-48 of the instant specification),

it is noted that the Diagnostic Reagents described on pages 42-43 of the instant specification appears more limited in its description of using antibodies to PSGL for the detection of human disorders in which P-selectin ligand might be defective.

Therefore, the election of the specific disorder involves defective binding of the leukocytes to activated platelets or endothelial cells, is under consideration in the instant application.

Claims 2-3 are pending and being acted upon.

3. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ® or ™ symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

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4. Claims 2-3 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-3 are indefinite in the recitation of "detecting a disorder involving defective binding of P-selectin glycoprotein ligand" and "wherein the disorder involves defective binding of the leukocytes to activated platelets or endothelial cells" because the nature and metes and bounds of said "disorder(s)" is ambiguous and ill-defined.

There is no or insufficient objective evidence that the ordinary artisan would have recognized the metes and bounds of said "disorder" or that the species or class of the claimed "disorders" was / were a class of disorders recognized in the art at the time the invention was made.

While paragraph [0088] on page 42 of the instant specification suggest patients with increase susceptibility to infections in which leukocytes might not be able to bind to activated platelets or endothelium,

there is little or no guidance as to defining the metes and bounds which infections or which patients with infections are encompassed by the claimed methods.

Further, claims 2-3 are indefinite and unclear in their recitation for being incomplete by omitting essential steps or ingredients, such omission amounting to a gap between the steps. See MPEP 2172.01.

For example, there appears insufficient steps and ingredients to carry out the methods of "detecting a disorder" by mere testing the binding the anti-PSLG-1 antibodies to leukocytes obtained from patients.

The claims do not forth clear, distinct and positive process steps with a step that clearly relates to the preamble of the claim. The nature of the "detecting a disorder" is not defined by the claim and, the specification does not provide a standard for ascertaining the requisite degree by which a disorder, including "wherein the disorder involves defective binding of the leukocytes to activated platelets or endothelial cells".

One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

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5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

In vitro and animal model studies have not correlated well with clinical diagnosis in patients. Since the detection of a disorder/disease can be disorder/disease-dependent, it is not clear that reliance on the in vitro and in vivo observations as well as the clinical experience with targeting various inflammatory conditions with anti-PSGL-1 antibodies accurately reflects the relative ability or efficacy of the claimed "methods to detect a disorder involving defective binding of P-selectin glycoprotein ligand in a patient"

In a review on the Role of PSGL-1 Binding to Selectins in Leukocyte Recruitment in McEver and Cummings, J. Clin. Invest. 100: S97-S103, 1997; the co-inventors conclude that:

"Many interesting questions remained to be answered. These include defining the details of the post-translational modifications that confer optimal PSGL-1 binding to selectins, the nature of the molecular contacts between lectin and ligand, the biophysical parameters that facilitate cell-cell interactions under flow, the molecular mechanism for PSGL-1-mediated leukocyte signaling and the role of PSGL-1-selectin interactions in vivo during physiological and pathological inflammation, hemostasis and hematopoiesis."

See entire document, including Conclusions on page S102.

Further, this J. Clin. Invest. Reference notes the broad Tissue Distribution of PSGL-1, including the observations that PSGL-1 is expressed differentially on leukocytes and this expression may differ in the same cell populations or that the PSGL-1 may be modified differentially among the leukocytes.

See Tissue Distribution of PSGL-1 on page S100.

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Several variables are used in evaluating the predictability of detection or diagnostic assays. These include diagnostic specificity and sensitivity and positive and negative predictive values.

The diagnostic sensitivity of an assay reflects the fraction of those subjects with a specific disease that the assay correctly identifies as positive.

The diagnostic specificity of an assay reflects the fraction of those subjects without the disease that the assay correctly identifies as negative.

The positive predictive value refers to the probability that an individual with a positive test result has the disease.

The negative predictive value refers to the probability that an individual with a negative test result does not have the disease.

There is an inverse relationship between the sensitivity and specificity, which is related to the assigned cutoff value that is used for a particular test to segregate diseased populations from those with no disease.

In the absence of objective evidence to the contrary and keeping with the nature of evaluating a number of potential immunological markers for diagnosis,

the skilled artisan would predict that there is an overlap between diseased and non-diseased groups, since individuals without a disease may exhibit abnormal levels of PSGL-1, while individuals with the disease may exhibit normal levels of PSGL-1.

Here, applicant has not provided sufficient direction and guidance as to the sensitivity and specificity of detecting a disorder involving defective binding of P-selectin glycoprotein ligand via the use of PSGL-1-specific antibodies alone.

Here, applicant has not set forth normal values as well as those values that would lead the skilled artisan to predict the ability to detect a disorder involving defective binding of P-selectin glycoprotein ligand via the use of PSGL-1-specific antibodies alone.

The cutoff value for a particular assay will determine the diagnostic sensitivity and specificity of the test based on the number of individuals that are diagnosed with and without the disease.

There is insufficient objective evidence that the claimed assay which relies upon the detection of PSGL-1 on leukocytes obtained from various patients provides the requisite sensitivity and specificity to be useful for the claimed purpose detecting a disorder involving defective binding of P-selectin glycoprotein ligand via the use of PSGL-1-specific antibodies alone.

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Further, as indicated above, given that the tissue distribution of PSGL-1 in leukocytes is broad and varies and that the role of PSGL-1-selectin interactions in vivo during physiological and pathological inflammation, hemostasis and hematopoiesis remained to be answered subsequent to applicant's priority dates,

the specification does not describe nor enable "methods of detecting a disorder involving defective binding of P-selectin glycoprotein ligand via the use of PSGL-1-specific antibodies" alone, commensurate in scope with the claimed invention.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

It does not appear that there is sufficient information to set forth the particular PSGL-1 levels, which correlates to a particular disorder, such that a particular disease is detected. The specification does not teach how to extrapolate data obtained from the expression or varying levels of expression of PSGL-1 in leukocytes obtained from patients can be significantly correlated to a particular disorder, including patients with increased susceptibility to infections (e.g., see paragraph [0088] on page 42 of the instant specification), commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the correlations of PSGL-1 in a patient's leukocytes to detect or to diagnose a disorder or a disease, broadly encompassed by the claimed methods. There is insufficient guidance and direction as well as objective evidence to provide for detecting or diagnosing the diversity and scope of disorders / diseases encompassed by the claimed methods.

In view of the lack of predictability of the art to which the invention pertains the lack of established protocols for effective methods to detect or diagnose the scope of inflammatory conditions, disorders and/or diseases with PSGL-1-specific antibody-based assays, undue experimentation would be required to practice the claimed methods of detecting a disorder involving defective binding of PSGL-1 with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for detecting a disorder involving defective binding of PSGL-1 via monitoring a patient's leukocytes with PSGL-1-specific antibodies alone, broadly encompassed by the claimed methods.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

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The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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